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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,419	08/08/2001	Jamie Rossjohn	3991/OJ678	9005

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DARBY & DARBY P.C.
P. O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER
MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,419	ROSSJOHN ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,8,11-34 and 36-46* is/are pending in the application.

4a) Of the above claim(s) *12-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-6, 8, 11, 32-34, 36-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/18/2006 has been entered.

2. Claim 10 has been canceled (5/18/2006). Amended claims 1, 2, 4-6, 18, 32-34, 36-40 (10/6/2005), previous claims 8, 11, and new claims 41-46 (5/18/2006) are under consideration.

3. Receipt of applicant's arguments and amendments filed on 5/18/2006 is acknowledged.

4. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 5/18/2006:

(i) the 35 USC 11, first paragraph new matter rejection over claims 1, 32; Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection ; and

(ii) the rejection of claims 1-2, 4-6, 8, 10, 11, 32-34, 36-40, under 35 U.S.C. 112, first paragraph, for the recitation of "human"; Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection; and

(iii) the rejection of claims 1-6, 8, 10-11, 32-35 under 35 U.S.C. 112, second paragraph. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

5. Applicant's arguments filed on 5/18/2006 have been fully considered and were persuasive in part. The issues remaining as well as new issues are stated below.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim rejections-35 USC § 112, first paragraph

7. Claims 1, 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claim 1, lines 6 and 8, recite "combination thereof" which language is new matter in the claim, since the instant specification fails to disclose such a limitation. The specification fails to provide proper support for this language in the claims for the following reason:

The specification on page 10, lines 35-38, recites:

"Preferably the portion of a the B'-C' loop of the domain includes Tyr 365, Ile 368 and His 367. GCSFR, GHR, and PRLR have an aromatic residue equivalent to Tyr 365, whereas there is no corresponding residue to His 367."

However, there is no mention in the specification as to a combination of these amino acid residues as recited in the amended.

Similarly, there is insufficient description for the limitation "a combination thereof" as recited in amended claim 1, line 8. Amended claim 32 recites this limitation which language is new matter in the claim, since the instant specification fails to disclose such a limitation. The

specification on page 11, lines 7-11, fails to provide proper support for this language in the claims for the following reason:

"The F'-G' loop adopts a type IV β turn at its tip in D4βc and the most significant features in this region are Arg 418 and Tyr 421, each of which projects out of solution (Fig. 1A). Accordingly, when the cytokine interacts with the βc chain, the Tyr 421 may interact with Domain 3 of βc and/or the α-chain to enhance receptor-receptor interaction or oligomerisation."

The specification does not disclose the specific limitations recited in amended claim 1. Similarly, amended 6, line 6, fails to find support in the specification for the limitation "a combination thereof". This rejection can only be obviated by reciting the specific limitations for which there are support in the instant specification.

8. Claims 1-2, 4-6, 8, 11, 32-34, 36-46, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons of record set forth at pages 4-7 of the previous Office action (6/6/2005) and pages 4-5 of the office action (11/18/2005).

The written description in this case only sets forth the specific residues 338-438 of $D4\beta_c$ which residues were expressed using the pEC611 vector in *E. coli* and that an antibody BION-1 MoAb raised against $D4\beta_c$ was used to obtain crystals of the antibody and $D4\beta_c$. The written description fails to describe the N-terminal section. The structure as shown in Figures 1A, B, C, D is described in the "Brief Description of the Drawings as follows:

Figure 1 illustrates the structure of D4βc. (A) Structure of the Fab/receptor βc domain 4 (D4βc) complex shown in ribbon representation. The MoAb heavy chain is shown in dark grey, the light chain and the receptor in light grey. The major structural features of D4βc are labeled and the locations of key residues are denoted by stick representation. These pictures were produced using Molscript (Kraulis, 1991) and Raster3D (Merritt and Murphy, 1994). (B) Structure as for (A) but reoriented 90* about the vertical axis. (C) Surface representation of the receptor using the program GRASP 35. The dark surface indicates the location of hydrophobic/aromatic patch, H1. The molecule is tilted approximately 20 degrees counterclockwise relative to (A). (D) View of hydrophobic/aromatic patch, H2 prepared as for (C). The molecule is tilted approximately 20 degrees clockwise and rotated approximately 60 degrees clockwise from above about a vertical axis relative to (B)."

This is insufficient description to support the claims to an "N-terminal section having the structure as shown in Figures 1A, B, C, D" as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Applicants argue that the claims have been amended to incorporate the language in the specification. However, contrary to Applicants arguments, the issue here is that the specification fails to recite the amino acid residues that are part of the N-terminal section of the domain being claimed. Therefore, Applicants have failed to obviate the standing 35 USC 112, first paragraph, written description rejection over claims 1-2, 4-6, 8, 11, 32-34, 36-46.

9. Claims 1-2, 4-6, 8, 11, 32-34, 36-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated cytokine-binding domain of

Domain 4 of a βc chain (D4βc) of a human cytokine receptor selected from the croup consisting of GM-CSF receptor, IL-3 receptor said domain consisting of amino acid residues 338-421 of D4βc, does not reasonably provide enablement for an isolated cytokine-binding domain of Domain 4 of a βc chain (D4βc) of a human cytokine receptor as recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1, for example, is overly broad in its limitation of "comprising a portion of the B'-C' loop of D4βc" and a "groove defined by the B'-C', the F'-G' loops comprising any one of the following residues..." because no guidance is provided as to which of the amino acids in the domain encompassed by the claims will encompass the peptide domain which retains the characteristics of the desired domain which binds the respective cytokine. Variants of a nucleic acid can be generated by deletions, insertions, and substitutions of nucleotides, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed domain protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches

that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use a domain peptide as recited in claim 1 other than the peptide consisting of amino acid residues 338-421 of D4βc, exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

10. Claims 1-2, 4-6, 8, 11, 32-34, 36-46, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as vague and indefinite for several reasons.

Claim 1, line 5, is vague and indefinite because it recites "comprising any one of...." Rather than "wherein said portion of the B'-C' loop comprises....".

Claim 1, line 7, is vague and indefinite because it is unclear whether the groove is defined by the B'-C' loop, the F'-G' loop and the N-terminal section or only by the B'-C' loop and the F'-G' loop. It is also unclear what the F'-G' loop is defined by. Does the F'-G' loop encompass the N-terminal section as recited in claim 1, lines 7-10? Furthermore, claim 2 recites that the F'-G' loop comprises "Arg 418....and the N-terminal section...". It is suggested that the claims be amended to properly define the loops, for which limitations there is a basis in the instant specification.

Claim 1, line 7, is vague and indefinite because it recites "a groove defined by the B'-C', the F'-G' loops....". However, the claim 1, line 9, the B'-C' loop, F'-G' loop and groove are recited independent of each other. Therefore, it is unclear which loops and which sections define the "groove".

Claim 1, line 7, is improper because it fails to recite "B'-C' loop".

Claim 1, line 9, is vague and indefinite because it recites "having" and it is unclear whether this is open or closed language. It is suggested that the claim be

amended to recite the conventional "consisting of" which is closed language or "comprising" which is open language.

Claims 36, 37, 38, 39, 40, line 1, are vague and indefinite because they recite "cytokine binding domain" rather than "cytokine-binding domain" as recited in the previous claims.

Claim 39 recites the limitation "the type 1 β-turn" in line 2. There is insufficient antecedent basis for this limitation in claim 1.

Claim 40, is vague and indefinite because it recites "Arg 418... as shown in Figure 1A". However, there is no Arg 418 indicated in Figure 1A.

Regarding claim 42, the phrase "characterized by" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "or the like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

Claim 46, line 1, is vague and indefinite because it recites "consists essentially of residues 338-421...", which limitation is vague and indefinite because it is unclear whether the residues are 330-420, 340-450 or something else. It is suggested that the claim be amended to delete this limitation n order to obviate this rejection.

Claim 4, 5, 6, 8, 11, 33-34, 41, 43-45, are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim rejections-35 USC § 102

11a. Claims 1-2, 4-6, 11, 32-34, 36-46 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/07215.

This rejection is maintained for reasons of record set forth at page 9 of the previous Office action (6/6/2005) and pages 6-7 of the office action (11/18/2005).

Applicants argue that the present claims recite "an isolated cytokine domain of domain 4 of a βc chain (D4βc) of a human cytokine receptor" and that in contrast to the present invention WO 97/07215 does not disclose or suggest use of the isolated D4βc, nor any specific domain structure thereof involved in cytokine-binding. However, contrary to Applicants arguments, the metes and bounds of "cytokine-binding domain" are unclear because of the terms "comprising a portion of the B'-C' loop" and "comprising any one of the following residues" in claim 1. The recitation of "comprising" encompasses the receptor used for identifying agonists to D4βc as recited in the WO 97.07215 reference.

Furthermore, Applicants argue that:

"Although WO 97/072 l 5 refers to the modeled structure of D4βc and contains a description of the modeling of D4βc structure, this was not done by the X-ray crystallography of D4βc itself as disclosed in the present application, but rather was deduced on the basis of the crystal coordinates of a different protein, a growth hormone binding protein (GHBP) (WO 97/07215, p. 11, 1ines. 1-7, Fig. 5). Specifically, in WO 97/07215, the βc chain sequence was aligned with domain 2 of GHBP and computer modeling was used to predict the structure of the D4βc (WO 97/07215 , pp. 8-9, 1ines 35-2, Fig. 5). Such an indirect method produces only an approximation of the D4βc structure, which is different from the D4βc cytokine binding domain structure disclosed and claimed in the present application. Indeed, the "groove" identified and determined by the Applicants as part of D4βc is absent from the predicted structure shown in Figure 5 of WO 97/07215."

However, contrary to Applicants arguments, it is irrelevant how the structure of D4βc was determined in the prior art. In the instant claims a product is being claimed, not a process, and based on the breadth of the instant claims while giving the instant claims their broadest possible interpretation, the prior art D4βc product meets the limitations of the instant claims. The "groove" claimed by Applicants in instant claim 1 is unclear. Furthermore, the entire domain structure being claimed by Applicants in instant claim 1 is unclear. The prior art on page 6, lines 6-16, discloses that the agent agonist of the GM-CSF, IL-3 and IL-5 receptors may be a peptide and discloses the D4βc structure as claimed in the instant invention. Therefore, the reference anticipates claims 1-2, 4-6, 11, 32-34, 36-46.

9b. Claims 1-2, 4-6, 10-11, 32-34, 36-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Woodcock et al. (1997).

This rejection is maintained for reasons of record set forth at pages 9-10 of the previous Office action (6/6/2005) and page 7 of the office action (11/18/2005).

Applicants argue that the claims have been amended to recite "an isolated cytokine domain of domain 4 of a βc chain (D4βc) of a human cytokine receptor" and that in contrast to the present invention Woodcock does not disclose or suggest use of the isolated D4βc, nor any specific domain structure thereof involved in cytokine-binding. However, contrary to Applicants arguments, the disclosure in the reference meets the limitations of the instant claims because the reference discloses an isolated cytokine-binding domain of a βc chain of human IL-3 receptor. Instant claim 1 recites "comprising any one of the following residues" which recitation encompasses the entire βc chain. Furthermore, the absence of the recitation in the claims of a specific contiguous region of the amino acid sequence of the D4βc chain (Applicants have only

recited specific amino acid residues within the entire domain), the reference anticipates the claims because the metes and bounds of the cytokine-binding domain being claimed are unclear. Therefore, the reference anticipates claims 1-2, 4-6, 11, 32-34, 36-46.

Conclusion

No claim is allowed.

Claims 1-2, 4-6, 8, 11, 32-34, 36-46 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
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